

FEE TRANSMITTAL

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT

\$1,120

Complete if Known

Patent Number	U.S. Patent 5,719,147
Issue Date	February 17, 1998
First Named Inventor	Conrad P. Dorn
Examiner Name	
Group Art Unit	
Attorney Docket Number	

METHOD OF PAYMENT (Check one)

☒ Deposit Account

Deposit Account Number

13-2755

Deposit Account Name

Merck & Co., Inc.

The Commissioner is authorized to:

☒ Charge fee(s) indicated below ☒ Credit any overpayments

☒ Charge any additional fee(s) during the pendency of this application

FEE CALCULATION

1. BASIC FILING FEE

Large Fee Code	Entity Fee (\$)	Fee Description	Fee Paid
1001	750	Utility filing fee	
1002	330	Design filing fee	
1004	750	Reissue filing fee	
1005	160	Provisional filing fee	

SUBTOTAL(1)

\$0

2. EXTRA CLAIM FEES

Total Claims	Extra	Fee from below	Fee Paid
20	** =	0 x \$18 =	0
3	** =	0 x \$84 =	0
Multiple Dependent Claims		\$280 =	

**or number previously paid, if greater; For Reissues, see below

Large Fee Code	Entity Fee (\$)	Fee Description
1202	18	Claims in excess of 20
1201	84	Independent claims in excess of 3
1203	280	Multiple dependent claim, if not paid
1204	84	**Reissue independent claims over original patent
1205	18	**Reissue claims in excess of 20 and over original patent

SUBTOTAL(2)

\$0

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Fee Code	Large Entity Fee (\$)	Fee Description	Fee Paid
1051	130	Surcharge - late filing fee or oath	
1812	2,520	For filing a request for <i>ex parte</i> reexamination	
1251	110	Extension for reply within first month	
1252	410	Extension for reply within second month	
1253	930	Extension for reply within third month	
1254	1,450	Extension for reply within fourth month	
1255	1,970	Extension for reply within fifth month	
1401	320	Notice of Appeal	
1402	320	Filing a brief in support of an appeal	
1403	280	Request for oral hearing	
1452	110	Petition to revive - unavoidable	
1453	1,300	Petition to revive - unintentional	
1501	1,300	Utility issue fee (or reissue)	
1502	470	Design issue fee	
1460	130	Petitions to the Commissioner	
1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	Submission of Information Disclosure Statement	
8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	For each additional invention to be examined (37 CFR 1.129(b))	
1801	750	Request for Continued Examination (RCE)	
Other fee (specify)		Extension of Term of Patent	1,120
		(37 C.F.R. 1.20(j)(i))	
SUBTOTAL(3)			\$1,120

SUBMITTED BY

Complete (if applicable)

Typed or Printed Name

J. Eric Thies

Reg. Number

35,382

Signature

J. Eric Thies

Date

05/16/2003

Deposit Account User ID

12

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re:	U.S. Patent 5,719,147
Issued:	February 17, 1998
To:	Conrad P. Dorn, et al.
Assignee:	Merck & Co., Inc.
For:	MORPHOLINE AND THIOMORPHOLINE TACHYKININ RECEPTOR ANTAGONISTS

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P.O. Box 1450
Alexandria, VA 22313-1450

APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. § 156

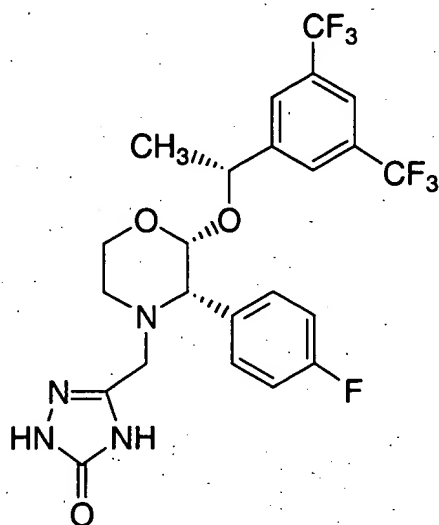
Sir:

Your Applicant, Merck & Co., Inc. a corporation organized and existing under the laws of the state of New Jersey, represents that it is the assignee of the entire interest in and to Letters Patent of the United States No. 5,719,147 granted to Conrad P. Dorn, et al. on February 17, 1998 for "Morpholine and Thiomorpholine Tachykinin Receptor Antagonists" by virtue of an assignment in favor of Merck & Co., Inc. recorded September 8, 1997, Reel 8717, Frame 0571.

Your Applicant acting through its duly authorized attorney, hereby submits this application for extension of patent term under 35 U.S.C. § 156 by providing the following information required by the rules promulgated by the U.S. Patent and Trademark Office (37 C.F.R. § 1.740). A copy of the Power of Attorney authorizing Mr. J. Eric Thies to act on behalf of your Applicants is attached hereto as "Attachment A." For the convenience of the U.S. Patent and Trademark Office, the information contained in this application is presented in a format that follows the order of requirements of 37 C.F.R. § 1.740.

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02 55:257 1120.00 EA

(a)(1) The approved product EMEND[®] (aprepitant) is a substance P/neurokinin 1 (NK₁) receptor antagonist and contains as the active ingredient aprepitant, having the chemical name 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluorophenyl)-4-(3-(5-oxo-1H,4H-1,2,4-triazolo)methylmorpholine or 5-[[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)-phenyl]ethoxy]-3-(4-fluorophenyl)-4-morpholinyl)methyl]-1,2-dihydro-3H-1,2,4-triazol-3-one. The structural formula for aprepitant is as shown below:



(2) The approved product was subject to regulatory review under the Federal Food, Drug and Cosmetic Act, Section 505 (21 U.S.C. § 355).

(3) The approved product, EMEND[®] (aprepitant) received permission for commercial marketing or use under Section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355) on March 26, 2003.

(4) The only active ingredient in EMEND[®] is aprepitant which has not been previously approved for commercial marketing or use under Section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355) prior to the approval of NDA 21-549 by the Food and Drug Administration on March 26, 2003.

(5) This Application for extension of patent term under 35 U.S.C. § 156 is being submitted within the permitted 60-day period pursuant to 37 C.F.R. § 1.720(f), said period which will expire on May 25, 2003.

(6) The complete identification of the patent for which extension is being sought is as follows:

Inventors: Conrad P. Dorn, Paul E. Finke, Jeffrey J. Hale, Malcolm MacCoss, Sander G. Mills, Shrenik K. Shah, Mark Stuart Chambers, Timothy Harrison, Tamara Ladduwahetty and Brian John Williams

Patent Number: 5,719,147

Date of Issue: February 17, 1998

Current Date of Expiration: June 29, 2012.

(7) See "Attachment B" for a complete copy of the patent identified in paragraph (6) hereof.

(8) No disclaimer, certificate of correction or reexamination certificate has been issued with regard to US Patent No. 5,719,147. The Maintenance Fee Statement for U.S. Patent No. 5,719,147 is attached hereto as "Attachment C" and indicates that the fourth year maintenance fee was duly paid.

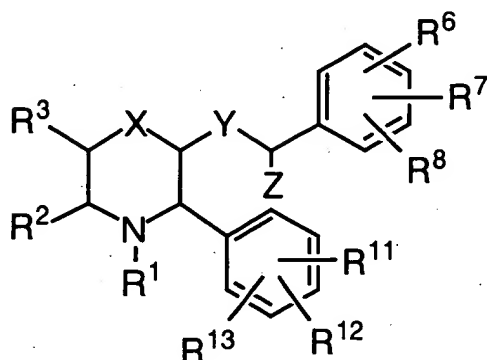
(9) U.S. Patent No. 5,719,147 claims the approved product and a method of using the approved product.

A listing of each applicable patent claim is: the active ingredient, aprepitant, is claimed as a compound in Claims 1, 2, 3, 4, 5, 6, 7, 9, 11, 15, 16 and 17; the active ingredient, aprepitant, is claimed as a pharmaceutical composition in Claims 18 and 19; and a method of using the active ingredient, aprepitant, is claimed in Claims 20 and 26.

(9)(i) The following analysis demonstrates the manner in which at least one such patent claim (e.g. Claim 1) reads on the approved product.

Claim 1 reads as follows:

1. A compound of the structural formula:



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from the group consisting of:

- (1) hydrogen;
- (2) C₁₋₆ alkyl, unsubstituted or substituted with one or more of the substituents selected from:
 - (a) hydroxy,
 - (b) oxo,
 - (c) C₁₋₆ alkoxy,
 - (d) phenyl-C₁₋₃ alkoxy,
 - (e) phenyl,
 - (f) -CN,
 - (g) halo, wherein halo is fluoro, chloro, bromo or iodo,
 - (h) -NR⁹R¹⁰, wherein R⁹ and R¹⁰ are independently selected from:
 - (i) hydrogen,
 - (ii) C₁₋₆ alkyl,
 - (iii) hydroxy-C₁₋₆ alkyl, and
 - (iv) phenyl,
 - (i) -NR⁹COR¹⁰,
 - (j) -NR⁹CO₂R¹⁰,
 - (j) -NR⁹CO₂R¹⁰,
 - (k) -CONR⁹R¹⁰,

- (l) -COR⁹,
- (m) -CO₂R⁹,
- (n) heterocycle, wherein the heterocycle is selected from the group consisting of:
 - (A) benzimidazolyl,
 - (B) benzofuranyl,
 - (C) benzothiophenyl,
 - (D) benzoxazolyl,
 - (E) furanyl,
 - (F) imidazolyl,
 - (G) indolyl,
 - (H) isooxazolyl,
 - (I) isothiazolyl,
 - (J) oxadiazolyl,
 - (K) oxazolyl,
 - (L) pyrazinyl,
 - (M) pyrazolyl,
 - (N) pyridyl,
 - (O) pyrimidyl,
 - (P) pyrrolyl,
 - (Q) quinolyl,
 - (R) tetrazolyl,
 - (S) thiadiazolyl,
 - (T) thiazolyl,
 - (U) thienyl,
 - (V) triazolyl,
 - (W) azetidiny,
 - (X) 1,4-dioxanyl,
 - (Y) hexahydroazepinyl,
 - (Z) piperazinyl,
 - (AA) piperidinyl,
 - (AB) pyrrolidinyl,
 - (AC) tetrahydrofuranyl, and
 - (AD) tetrahydrothienyl,

and wherein the heterocycle is unsubstituted or substituted with one or more substituent(s) selected from:

- (i) C₁₋₆ alkyl, unsubstituted or substituted with halo, -CF₃, -OCH₃, or phenyl,
- (ii) C₁₋₆ alkoxy,
- (iii) oxo,
- (iv) hydroxy,
- (v) thioxo,
- (vi) -SR⁹,
- (vii) halo,
- (viii) cyano,
- (ix) phenyl,
- (x) trifluoromethyl,
- (xi) -(CH₂)_m-NR⁹R¹⁰, wherein m is 0, 1 or 2,
- (xii) -NR⁹COR¹⁰,
- (xiii) -CONR⁹R¹⁰,
- (xiv) -CO₂R⁹, and
- (xv) -(CH₂)_m-OR⁹;

(3) C₂₋₆ alkenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:

- (a) hydroxy,
- (b) oxo,
- (c) C₁₋₆ alkoxy,
- (d) phenyl-C₁₋₃ alkoxy,
- (e) phenyl,
- (f) -CN,
- (g) halo,
- (h) -CONR⁹R¹⁰,
- (i) -COR⁹,
- (j) -CO₂R⁹,
- (k) heterocycle;

(4) C₂₋₆ alkynyl;

(5) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:

- (a) hydroxy,
- (b) C₁₋₆ alkoxy,
- (c) C₁₋₆ alkyl,
- (d) C₂₋₅ alkenyl,
- (e) halo,
- (f) -CN,
- (g) -NO₂,
- (h) -CF₃,
- (i) -(CH₂)_m-NR⁹R¹⁰,
- (j) -NR⁹COR¹⁰,
- (k) -NR⁹CO₂R¹⁰,
- (l) -CONR⁹R¹⁰,
- (m) -CO₂NR⁹R¹⁰,
- (n) -COR⁹, and
- (o) -CO₂R⁹;

R² and R³ are independently selected from the group consisting of:

- (1) hydrogen,
- (2) C₁₋₆ alkyl, unsubstituted or substituted with one or more of the substituents selected from:

- (a) hydroxy,
- (b) oxo,
- (c) C₁₋₆ alkoxy,
- (d) phenyl-C₁₋₃ alkoxy,
- (e) phenyl,
- (f) -CN,
- (g) halo,
- (h) -NR⁹R¹⁰,
- (i) -NR⁹COR¹⁰,
- (j) -NR⁹CO₂R¹⁰,
- (k) -CONR⁹R¹⁰,
- (l) -COR⁹, and

- (m) $-\text{CO}_2\text{R}^9$;
- (3) C₂₋₆ alkenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
- (a) hydroxy,
 - (b) oxo,
 - (c) C₁₋₆ alkoxy,
 - (d) phenyl-C₁₋₃ alkoxy,
 - (e) phenyl,
 - (f) $-\text{CN}$,
 - (g) halo,
 - (h) $-\text{CONR}^9\text{R}^{10}$,
 - (i) $-\text{COR}^9$, and
 - (j) $-\text{CO}_2\text{R}^9$;
- (4) C₂₋₆ alkynyl;
- (5) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
- (a) hydroxy,
 - (b) C₁₋₆ alkoxy,
 - (c) C₁₋₆ alkyl,
 - (d) C₂₋₅ alkenyl,
 - (e) halo,
 - (f) $-\text{CN}$,
 - (g) $-\text{NO}_2$,
 - (h) $-\text{CF}_3$,
 - (i) $-(\text{CH}_2)_m-\text{NR}^9\text{R}^{10}$,
 - (j) $-\text{NR}^9\text{COR}^{10}$,
 - (k) $-\text{NR}^9\text{CO}_2\text{R}^{10}$,
 - (l) $-\text{CONR}^9\text{R}^{10}$,
 - (m) $-\text{CO}_2\text{NR}^9\text{R}^{10}$,
 - (n) $-\text{COR}^9$, and
 - (o) $-\text{CO}_2\text{R}^9$;

R⁶, R⁷ and R⁸ are independently selected from the group consisting of:

- (1) hydrogen;
- (2) C₁₋₆ alkyl, unsubstituted or substituted with one or more of the substituents selected from:
 - (a) hydroxy,
 - (b) oxo,
 - (c) C₁₋₆ alkoxy,
 - (d) phenyl-C₁₋₃ alkoxy,
 - (e) phenyl,
 - (f) -CN,
 - (g) halo,
 - (h) -NR⁹R¹⁰,
 - (i) -NR⁹COR¹⁰,
 - (j) -NR⁹CO₂R¹⁰,
 - (k) -CONR⁹R¹⁰,
 - (l) -COR⁹, and
 - (m) -CO₂R⁹;
- (3) C₂₋₆ alkenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
 - (a) hydroxy,
 - (b) oxo,
 - (c) C₁₋₆ alkoxy,
 - (d) phenyl-C₁₋₃ alkoxy,
 - (e) phenyl,
 - (f) -CN,
 - (g) halo,
 - (h) -CONR⁹R¹⁰,
 - (i) -COR⁹, and
 - (j) -CO₂R⁹;
- (4) C₂₋₆ alkynyl;
- (5) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
 - (a) hydroxy,
 - (b) C₁₋₆ alkoxy,

- (c) C₁₋₆ alkyl,
 - (d) C₂₋₅ alkenyl,
 - (e) halo,
 - (f) -CN,
 - (g) -NO₂,
 - (h) -CF₃,
 - (i) -(CH₂)_m-NR⁹R¹⁰,
 - (j) -NR⁹COR¹⁰,
 - (k) -NR⁹CO₂R¹⁰,
 - (l) -CONR⁹R¹⁰,
 - (m) -CO₂NR⁹R¹⁰,
 - (n) -COR⁹, and
 - (o) -CO₂R⁹;
- (6) halo,
 - (7) -CN,
 - (8) -CF₃,
 - (9) -NO₂,
 - (10) -SR¹⁴, wherein R¹⁴ is hydrogen or C₁₋₅alkyl,
 - (11) -SOR¹⁴,
 - (12) -SO₂R¹⁴,
 - (13) NR⁹COR¹⁰,
 - (14) CONR⁹COR¹⁰,
 - (15) NR⁹R¹⁰,
 - (16) NR⁹CO₂R¹⁰,
 - (17) hydroxy,
 - (18) C₁₋₆alkoxy,
 - (19) COR⁹,
 - (20) CO₂R⁹,
 - (21) 2-pyridyl,
 - (22) 3-pyridyl,
 - (23) 4-pyridyl,
 - (24) 5-tetrazolyl,
 - (25) 2-oxazolyl, and
 - (26) 2-thiazolyl;

R¹¹, R¹² and R¹³ are independently selected from the definitions of R⁶, R⁷ and R⁸;

X is selected from the group consisting of:

- (1) -O-,
- (2) -S-,
- (3) -SO-, and
- (4) -SO₂-;

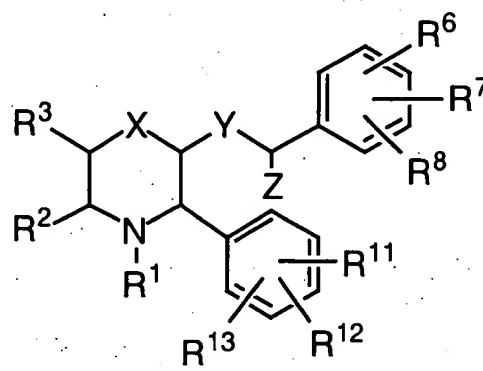
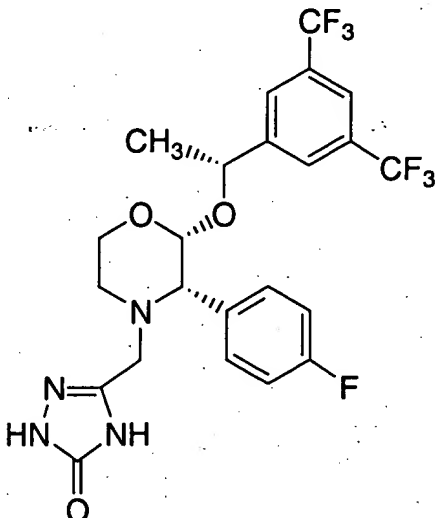
Y is selected from the group consisting of:

- (1) a single bond,
- (2) -O-,
- (3) -S-,
- (4) -CO-,
- (5) -CH₂-,
- (6) -CHR¹⁵-, and
- (7) -CR¹⁵R¹⁶-, wherein R¹⁵ and R¹⁶ are independently selected from the group consisting of:
 - (a) C₁₋₆ alkyl, unsubstituted or substituted with one or more of the substituents selected from:
 - (i) hydroxy,
 - (ii) oxo,
 - (iii) C₁₋₆ alkoxy,
 - (iv) phenyl-C₁₋₃ alkoxy,
 - (v) phenyl,
 - (vi) -CN,
 - (vii) halo,
 - (viii) -NR⁹R¹⁰,
 - (ix) -NR⁹COR¹⁰,
 - (x) -NR⁹CO₂R¹⁰,
 - (xi) -CONR⁹R¹⁰,
 - (xii) -COR⁹, and
 - (xiii) -CO₂R⁹;

(b) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:

- (i) hydroxy,
- (ii) C₁₋₆ alkoxy,
- (iii) C₁₋₆ alkyl,
- (iv) C₂₋₅ alkenyl,
- (v) halo,
- (vi) -CN,
- (vii) -NO₂,
- (viii) -CF₃,
- (ix) -(CH₂)_m-NR⁹R¹⁰,
- (x) -NR⁹COR¹⁰,
- (xi) -NR⁹CO₂R¹⁰,
- (xii) -CONR⁹R¹⁰,
- (xiii) -CO₂NR⁹R¹⁰,
- (xiv) -COR⁹, and
- (xv) -CO₂R⁹;

Z is C₁₋₆ alkyl.

The structural formula of the compound of Claim 1 is:	Aprepitant is represented by the following structural formula:
	

The approved product contains aprepitant which is a compound of Claim 1 wherein:

- R¹ is C₁₋₆ alkyl, substituted with a substituent which is a heterocycle, wherein the heterocycle is triazolyl, and wherein the triazolyl is substituted with oxo;
- R² is hydrogen,
- R³ is hydrogen,
- R⁶ is -CF₃;
- R⁷ is -CF₃;
- R⁸ is hydrogen;
- R¹¹ is halo, wherein halo is fluoro;
- R¹² is hydrogen;
- R¹³ is hydrogen;
- X is -O-;
- Y is -O-; and
- Z is C₁₋₆ alkyl.

(9)(ii) The following analysis demonstrates the manner in which at least one such patent claim (e.g. Claim 26) reads on the method of using the approved product, where the claims include any claim to the method of using the approved product.

Claim 26 reads as follows:

26. A method for the treatment or prevention of emesis in a mammal in need thereof which comprises the administration to the mammal of an effective amount of the compound of Claim 1.

The approved product EMEND[®] (aprepitant) is a substance P/neurokinin 1 (NK₁) receptor antagonist and has been approved for the prevention of acute and delayed nausea and vomiting (which is emesis) associated with initial and repeat courses of highly emetogenic cancer chemotherapy, and contains as an active ingredient aprepitant which is a compound of Claim 1 as described under the above analysis for Claim 1.

(10) The relevant dates and information pursuant to 35 U.S.C. § 156(g) to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

(i)(A) Investigational New Drug Application (IND 50,283) for Aprepitant was submitted on April 9, 1996 and the IND became effective on May 9, 1996.

(B) New Drug Application (NDA 21-549) EMEND® (Aprepitant) was submitted on September 27, 2002; and

(C) New Drug Application (NDA 21-549) EMEND® (Aprepitant) was approved on March 26, 2003.

(11) As a brief description of the significant activities undertaken by Applicant, Merck & Co., Inc., during the applicable regulatory review period, attached hereto as "Attachment D", is a chronology of the major communications between the Applicant and the FDA from April 9, 1996 to March 26, 2003.

(12)(A) Applicant is of the opinion that U.S. Patent 5,719,147 is eligible for extension under 35 U.S.C. § 156 because it satisfies all of the requirements for such extension as follows:

(a) 35 U.S.C. § 156(a)

U.S. Patent 5,719,147 claims the approved product, a method of using the product and a method of manufacturing the product.

(b) 35 U.S.C. § 156(a)(1)

The term of U.S. Patent 5,719,147 has not expired before submission of this application under 35 U.S.C. § 156(d)(1) for its extension.

(c) 35 U.S.C. § 156(a)(2)

The term of U.S. Patent 5,719,147 has never been extended under 35 U.S.C. § 156(e)(1).

(d) 35 U.S.C. § 156(a)(3)

The application for extension is submitted by the owner of record and is in accordance with the requirement of 35 U.S.C. § 156(d) and rules of the U.S. Patent and Trademark Office.

(e) 35 U.S.C. § 156(a)(4)

The product, EMEND® (aprepitant), has been subject to a regulatory review period before its commercial marketing or use.

(f) 35 U.S.C. § 156(a)(5)(A)

The permission for the commercial marketing or use of the product, EMEND® (Aprepitant), after the regulatory review period is the first permitted commercial marketing or use of the product under the provision of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355) under which such regulatory review period occurred.

(g) 35 U.S.C. § 156(c)(4)

No other patent has been extended for the same regulatory review period for the product, EMEND® (Aprepitant).

(12)(B) The length of extension of the patent term of U.S. Patent 5,719,147 claimed by Applicant is 1022 days or approx. 2.8 years. The length of the extension was determined pursuant to 37 C.F.R. § 1.775 as follows:

(a) The regulatory review period under 35 U.S.C. 156(g)(1)(B) began on May 9, 1996 and ended on March 26, 2003 which is a total of 2512 days or 6.88 years which is the sum of (i) and (ii) below:

(i) The period of review under 35 U.S.C. 156(g)(2)(B)(i), the "Testing Period," began on May 9, 1996 and ended on September 26, 2002, which is 2332 days or 6.39 years and

(ii) The period of review under 35 U.S.C. 156(g)(2)(B)(ii), the "Application Period," began on September 27, 2002 and ended on March 26, 2003, which is 180 days or 0.49 years;

(b) The regulatory review period upon which the period of extension is calculated is the entire regulatory review period as determined in sub-paragraph (12)(B)(a) above (2512 days) less

(i) The number of days in the regulatory review period which were on or before the date on which the patent issued (May 9, 1996 to February 17, 1998) which is 649 days, and

(ii) The number of days during which applicant did not act with due diligence which is zero (0) days, and

(iii) One-half the number of days determined in sub-paragraph (12)(B)(a)(i) after the patent issued $[(2331 - 649)/2]$ or 841 days;

(iv) The regulatory period is calculated by subtracting the number of days determined in sub-paragraph (12)(B)(b)(i)-(iii) from the entire regulatory review period as determined in sub-paragraph (12)(B)(a) (which is 2512 days – 649 days – 0 days – 841 days) which equals 1022 days;

(c) The number of days as determined in sub-paragraph (12)(B)(b)(iv) (1040 days) when added to the original term of the patent (June 29, 2012, as determined by 35 U.S.C. § 154 (c) and 37 C.F.R. § 1.321) would result in the date, April 17, 2015;

(d) Fourteen (14) years when added to the date of NDA approval (March 26, 2003) would result in the date March 26, 2017;

(e) The earlier date as determined in sub-paragraphs (12)(B)(c) and (12)(B)(d) is April 17, 2015;

(f) Since the original patent was not issued and a request for an exemption was not submitted before September 24, 1984 and the commercial marketing or use of the product was not approved before September 24, 1984, five (5) years when added to the original expiration date of the patent (June 29, 2012) would result in the date, June 29, 2017;

(g) The earlier date as determined in sub-paragraph (12)(B)(e) and (12)(B)(f) is April 17, 2015.

(13) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought.


(14) The prescribed fee as set forth in 37 C.F.R. § 1.20(j)(1) for receiving and acting upon this application for extension is to be charged to Merck Deposit Account No. 13-2755 as authorized in the attached Fee Sheet, which is submitted in duplicate.

(15) Please address all inquiries and correspondence relating to the application for patent term extension to:

J. Eric Thies
Merck & Co., Inc.
Patent Department
P.O. Box 2000
Rahway, New Jersey 07065-0907
Telephone: (732) 594-3904
Facsimile: (732) 594-4720

(16) The instant application for extension of patent term with regard to U.S. Patent No. 5,719,147 is being submitted as one original and triplicate copies thereof.

Respectfully submitted,

By 
J. Eric Thies
Reg. No. 35,382
Attorney for Applicant

MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-3904


Date: May 16, 2003

Attachments:

- "Attachment A" - Power of Attorney
- "Attachment B" - Copy of U.S. Patent Number: 5,719,147
- "Attachment C" - Maintenance Fee Statement for U.S. Patent No. 5,719,147
- "Attachment D" - Chronology of Major Communications with the FDA
- Fee Sheet

CERTIFICATION

The undersigned hereby certifies that this application for extension of patent term under 35 U.S.C. § 156 including its attachments and supporting papers is being submitted as one original and triplicate copies thereof.

By 
J. Eric Thies
Reg. No. 35,382
Attorney for Applicant

MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-3904

Date: May 16, 2003

ATTACHMENT A

Associate Power of Attorney

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Conrad P. Dorn, et al.

Patent No.: U.S. Patent No. 5,719,147

Issued : February 17, 1988

For: MORPHOLINE AND THIOMORPHOLINE TACHYKININ
RECEPTOR ANTAGONISTS

Group Art Unit:

Examiner:

ASSOCIATE POWER OF ATTORNEY

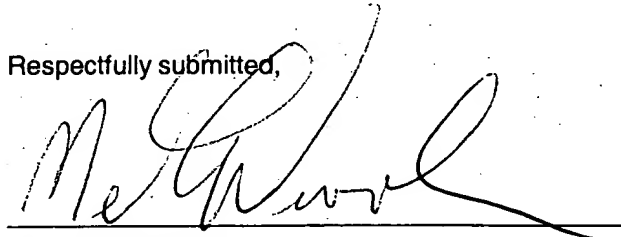
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In connection with the above-identified application the undersigned attorney and/or agent of record hereby appoints J. Eric Thies Registration No. 35,382 c/o MERCK & CO., INC., Patent Dept., RY60-30, P.O. Box 2000, Rahway, New Jersey 07065-0907, an associate attorney and/or agent, to prosecute this application, to make alterations and amendments therein, to receive the patent and to transact all business in the Patent and Trademark Office connected therewith.

All communications in connection with the prosecution of the above-identified application should be sent to J. Eric Thies c/o MERCK & CO., INC., Patent Dept., RY60-30, P.O. Box 2000, Rahway, New Jersey 07065-0907.

Respectfully submitted,



By: Melvin Winokur
Attorney for Applicant(s)

Reg. No. 32,763

(732)594- 7234

Date: May 16, 2003

General Corporate Resolution #5

PATENT MATTERS

RESOLVED, that any of the following:

Raymond V. Gilmartin-Chairman of the Board, President and Chief Executive Officer
Kenneth C. Frazier-Senior Vice President and General Counsel
Joseph F. DiPrima-Vice President and Assistant General Counsel
Paul D. Matukaitis-Vice President and Assistant General Counsel
Edward W. Murray-Counsel, Litigation
Charles M. Caruso-Counsel, International
Valerie J. Camara-Counsel, Patents
W. Gwyn Cole-Counsel, European Patents
Mark R. Daniel-Counsel, Patents
Joanne M. Giesser-Counsel, Patents
David L. Rose-Counsel, Patents
Jack L. Tribble-Counsel, Patents
Melvin Winokur-Counsel, Patents
Donna L. Margiotto-Senior Manager, Patent Administration


are authorized to execute and to revoke on behalf of Merck & Co., Inc. and its affiliates (including subsidiaries) the following documents relating to patent matters:

Powers of attorney as fully in law as may be necessary and proper in connection with the acquisition, registration, maintenance and enforcement of patents and applications for patents, including powers of attorney relating to the prosecution or defense of patent rights before courts of law or other governmental tribunals, agencies or departments; affidavits and declarations; and any other documents which are necessary and proper for the acquisition, registration, maintenance, litigation and protection of patents.

CERTIFICATION

I, Debra A. Bollwage, Assistant Secretary of Merck & Co., Inc., a Corporation duly organized and existing under the laws of the State of New Jersey, do hereby certify that the attached, presently in full force and effect, is a true and correct copy of General Corporate Resolution #5, Patent Matters, as amended by Unanimous Written Consent of the Board of Directors of said Corporation on April 23, 2002.

IN WITNESS WHEREOF, I have hereunto subscribed my signature and affixed the seal of the Corporation this 29th day of April, 2002.


Debra A. Bollwage
Assistant Secretary

(SEAL)

ATTACHMENT B

U.S. Patent No. 5,719,147

OTHER PUBLICATIONS

Lowe, et al., "The Discovery of (2S,3S)-cis-2(Diphenylmethyl)- N-(2-methoxyphenyl)methyl . . . ", *J. Med. Chem.*, vol. 35, pp. 2591-2600 (1992).
McCormick, "Properties of Penodate-Oxidised Polysaccharides", *J. Chem. Society*, vol. C(23), pp. 2121-2127 (1966).
Montgomery, et al., "2-Fluoropurine Ribonucleosides", *J. of Med. Chem.*, vol. 13(3), pp. 421-427 (1970).
Payan, et al., "Substance P. Recognition by a Subset of Human T Lymphocytes", *J. Clin. Invest.*, 74, 1532-1539 (1984).

Peyronel, et al., "Synthesis of RP-67,580, a New Potent Nonpeptide Substance P Antagonist", *Biorg. and Med. Chem. Lett.*, vol. 2(6), pp. 559-564 (1992).

Siemer, et al., "Analgesic 1-phenyl-2,3-dimethyl-4-morpholinomethyl-3-pyrazolin-5-ones . . . " *Chem. Abstracts*, 56, No. 6, No. 5977e (1962).

Chem. Abstracts, 113 (20) p. 123, No. 174441m (Nov. 12, 1990). "Amine Hydrochlorides—Catalysts for Hydrochlorination".

Laddlewahetty et al., *Bioorg. Med. Chem.*, 4(16) 1917-20, 1994.

ATTACHMENT C

U.S. Patent No. 5,719,147 Maintenance Fee Statement



UNITED STATES
PATENT AND
TRADEMARK OFFICE

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Page**Maintenance Fee Statement****5719147**

The data shown below is from the records of the Patent and Trademark Office. If the maintenance fees and any necessary surcharges have been timely paid for the patents listed below, the notation "PAID" will appear in column 11, "STAT" below.

If a maintenance fee payment is defective, the reason is indicated by code in column 11, "STAT" below. TIMELY CORRECTION IS REQUIRED IN ORDER TO AVOID EXPIRATION OF THE PATENT. NOTE 37 CFR 1.377. THE PAYMENT(S) WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION. IF PAYMENT OR CORRECTION IS SUBMITTED DURING THE GRACE PERIOD, A SURCHARGE IS ALSO REQUIRED. NOTE 37 CFR 1.20(k) and (l).

If the statement of small entity status is defective the reason is indicated below in column 10 for the related patent number. THE STATEMENT OF SMALL ENTITY STATUS WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION.

ITEM NBR	PATENT NUMBER	FEE CDE	FEE AMT	SUR CHARGE	SERIAL NUMBER	PATENT DATE	FILE DATE	PAY YR	SML ENT	STAT
1 000000	5,719,147	183	850	0	08/525,259	02/17/98	09/08/95	04	NO	PAID

ITEM NBR	ATTY DKT NUMBER
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1

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ATTACHMENT D

EMEND[®] (Aprepitant) Chronology of Major Communications with the FDA

Attachment D

**EMEND® (Aprepitant)
Chronology of Major Communications with the FDA**

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
000		09Apr1996	Original IND filed
X		19Apr1996	FDA Acknowledgment Letter - Original Investigational New Drug Application
X		06Jun1996	FDA Correspondence containing comments regarding initial IND protocol no. 002
003		13Jun1996	Protocol Amendment - Change in Protocol containing revised protocol no. 002.
X		15Aug1996	FDA Comments regarding CMC section of the Initial Investigational New Drug Application.
022		18Apr1997	General Correspondence, IND notification of initial export waiver.
X		23Apr1997	FDA Approval of initial export waiver.
028		13Jun1997	Submission of first Annual IND Progress Report
X		09Jul1997	FDA Comments regarding pharmacology reports and oral toxicology studies in rats and dogs (submissions dated 16Apr1996/Serial No. 001 and 29Aug1996/Serial No. 005).
034		07Aug1997	MRL Response to FDA comments dated 09Jul1997.
X		16Sep1997	FDA Response to 07May1997/Serial No. 026 and 19May1997/Serial No. 027 Pharmacology/Toxicology amendments regarding the MRL suggested rat carcinogenicity doses.
077		05Aug1998	Submission of second Annual IND Progress Report
082		03Nov1998	Information Amendment - Pharmacology/Toxicology (Dose Selection Rat and Mouse Oral Carcinogenicity Study) submission providing response to September 16, 1997. Agency response to MRL proposed doses for the oral rat carcinogenicity study.

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
X		09Feb1999	FDA Response to 03Nov1998 providing additional comment regarding carcinogenicity and requesting MRL response for discussion with the ECAC.
088		22Feb1999	MRL Request for End-of-Phase 2 Meeting.
089		02Mar1999	MRL Response to FDA Request for Information regarding carcinogenicity studies in rats and mice.
090		12Mar1999	MRL Request for Meeting with ECAC and Division representatives to discuss dose selection for the oral carcinogenicity studies in rats and mice.
091		18Mar1999	End-of-Phase 2 Background Package for 14Apr1999 meeting.
X		14Apr1999	End-of-Phase 2 Meeting MRL/FDA
X		14May1999	Receipt of FDA version of End-of-Phase 2 Meeting Minutes
093		08Jun1999	Submission of third Annual IND Progress Report
099		12Jul1999	MRL Response to the FDA version End-of-Phase 2 Meeting Minutes.
X		20Aug1999	FDA Response to 12Jul1999 MRL Comments regarding End-of-Phase 2 Meeting Minutes providing additional comments and recommendations.
X		02Sep1999	FDA Correspondence containing comments on proposed protocol no. 040 also discussed during the April 14, 1999 End-of-Phase 2 Meeting.
114		06Jan2000	Protocol Amendment - Change in Protocol providing a revised protocol no. 040 per FDA correspondence received September 2, 1999.
115		07Jan2000	MRL Response to FDA Response dated September 2, 1999 with a commitment to continue planned studies to address issues raised in the September 2, 1999 communication.
X		29Mar2000	Additional FDA comments on proposed Pharmacology/Toxicology studies.
131		12May2000	MRL Response to March 29, 2000 FDA Comments and notice of continued efforts at addressing issues involving safety

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
			assessment toxicity/toxicokinetic evaluations with MK-0869.
136		01Jun2000	Submission of fourth Annual IND Progress Report
142		21Jul2000	Request for End-of-Phase 2 Meeting
X		04Aug2000	FDA Confirmation of September 21, 2000 End-of-Phase 2 Meeting
150		05Sep2000	MRL End-of-Phase 2 Background Package
152		15Sep2000	MRL addendum to End-of-Phase 2 Background Package
X		21Sep2000	MRL/FDA End-of-Phase 2 Meeting
158		09Oct2000	MRL Request for Agency comment from the Division and the Office of Post-Marketing Drug Risk Assessment (OPDRA) on the proposed tradename EMEND.
163		19Oct2000	MRL Request for Agency comment on the proposed tradename EMEND attachment includes outline of proposed dosage strengths within labeling.
X		20Oct2000	FDA version of End-of-Phase 2 Meeting Minutes
164		26Oct2000	MRL updates to 19Oct2000 submission.
165		27Oct2000	MRL submission of Phase 3 protocol no. 052 with request for special assessment by Agency.
170		14Nov2000	MRL General Correspondence in follow-up to End-of-Phase 2 meeting discussions related to agreement that the Agency would be amenable to a waiver agreement that specifies that data collection of only serious adverse experiences in the multiple cycle extensions of the phase 3 protocols due to the complicated nature of the patients' health conditions.
X		14Dec2000	FDA meeting minutes 12Dec2000 from the meeting of the Executive Carcinogenesis Assessment Committee (ECAC).
X		03Jan2001	FDA Correspondence referencing the Agency's ECAC meeting minutes and pharmacology/toxicology MRL submissions dated 11Aug2000, serial no. 146.

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
X		05Jan2001	FDA Correspondence regarding Safety Reporting for MRL Phase 3 protocols.
192		21Mar2001	MRL Response to January 3, 2001 Request
193		29Mar2001	MRL submission of Data Analysis Plans for protocols 040, 042
X		26Apr2001	FDA response to MRL request dated October 27, 2000 for special protocol assessment of protocol no. 052.
198		09May2001	MRL Request for meeting to discuss ECAC Issues
X		11May2001	FDA Response to Request for Meeting indicating reconsideration of MRL's March 21, 2001 submission as acceptable. Meeting was deemed not necessary.
201		07Jun2001	Submission of fifth Annual IND Progress Report
206		06Jul2001	MRL Response to FDA Request for Information providing justification for the use of a cis ester intermediate as a starting material in the manufacture of MK-0869.
208		18Jul2001	MRL Response to April 30, 2001 FDA Comments on Protocol 052.
231		28Nov2001	MRL Request for PreNDA Meeting
			Response to FDA Request for Information containing updated outline of the proposed indication and dosage and administration of EMEND.
236		18Dec2001	MRL General Correspondence providing notification of MEC data within the NDA filing.
238		04Jan2002	Submission of PreNDA Background Package for January 22, 2002 meeting.
X		09Jan2002	FDA Confirmation of January 22, 2002 PreNDA Meeting for EMEND.
X		17Jan2002	FDA Response to PreNDA Background Package
X		22Jan2002	PreNDA meeting on January 22, 2002.
X		29Jan2002	FDA Correspondence regarding proposed tradename for EMEND.
X		11Feb2002	FDA Correspondence regarding PreNDA meeting minutes
245		15Feb2002	MRL Response to January 29, 2002 FDA Comments on Proposed Tradename,

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
			EMEND.
X		01Apr2002	FDA Correspondence regarding EMEND tradename.
255		18Apr2002	MRL response to agency request for an example SAS transport file format.
257		01May2002	MRL response to FDA request for information providing a copy of the slides presented by MRL at the PreNDA meeting on January 22, 2002.
258		04Jun2002	Submission of sixth Annual IND Progress Report
261		25Jun2002	MRL EMEND Trademark Appeal, Request for FDA Response.
262		27Jun2002	MRL Response to FDA Request for Information regarding the pediatric program.
	20Aug2002		Prescription Drug User Fee submission for original NDA (User Fee ID No. 4403).
X		23Aug2002	MRL/FDA teleconference to discuss the proposed tradename EMEND.
	27Sep2002		Original New Drug Application filing date.
269		16Oct2002	MRL Response to FDA Request for Information providing meeting minutes of the August 23, 2002 teleconference to discuss the tradename EMEND.
270	17Oct2002	17Oct2002	Formal Dispute Resolution Request providing chronology of events background package of EMEND tradename discussions submitted to Formal Dispute Resolution Project Manager at FDA. Also submitted as General Correspondence to IND.
	18Oct2002		Copy of Formal Dispute Resolution Request providing chronology of events background package of EMEND tradename discussions submitted to NDA as electronic archival copy.
X		18Oct2002	FDA Correspondence providing comment on MRL pediatric studies program.
X	25Oct2002	25Oct2002	FDA Acknowledgment of Formal Dispute Resolution Request received from Formal Dispute Resolution Project Manager, CDER.

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
X	28Oct2002		FDA Request for CMC Information related to NDA 21-549.
X	30Oct2002		FDA Correspondence related to tradename EMEND.
X	30Oct2002		FDA Approval of EMEND tradename provided MRL initiate a post-marketing risk management program similar to the one described in MRL's October 17, 2002 submission.
X	05Nov2002		MRL Response to Agency request dated October 28, 2002.
X	08Nov2002		FDA Request for Statistical/Safety Assessment Information related to NDA 21-549.
X	08Nov2002		FDA Acknowledgment of Receipt Letter for Original NDA 21-549, received September 27, 2002.
X	19Nov2002		Response to FDA Request for Information dated November 8, 2002.
X	22Nov2002		Response to FDA Request for Information dated November 8, 2002.
X	25Nov2002		Response to FDA Request for Information dated November 8, 2002.
X	03Dec2002		FDA Request for CMC Information
X	27Dec2002		MRL Response to December 3, 2002 Agency Request for CMC clarifications.
X	03Jan2003		FDA Request for Clinical Information
X	06Jan2003		MRL Request for Pre-Advisory Committee Meeting
X	07Jan2003		MRL Safety Update Report submitted to NDA 21-549.
X	15Jan2003		Response to FDA Request for Information January 9, 2003. Submission of Draft Advisory Committee Background Package.
X	23Jan2003		FDA Request for Clinical Information
X	23Jan2003		FDA Comments/Recommendations regarding draft advisory committee background package
X	24Jan2003		Pre-Advisory Committee Meeting with FDA.
X	30Jan2003		FDA Request for Clinical Information

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
X	31Jan2003		Submission of Final Advisory Committee Background Package for March 6, 2003 Advisory Committee Meeting.
X	06Feb2003		FDA Request for Statistical Information
X	12Feb2003		MRL Response to January 23, 2003 Request for Information
X	12Feb2003		MRL Response to January 30, 2003 Request for Information
X	12Feb2003		MRL Response to February 6, 2003 Statistical Request for Information, Part 1.
X	12Feb2003		MRL Response to Agency Request for CINV specific investigator list.
X	14Feb2003		MRL Response to February 6, 2003 Statistical Request for Information, Part 2.
278		13Feb2003	Response to FDA Request for Information providing a copy of the DDMAC background package dated August 16, 2002.
X	20Feb2003		Agency response to Advisory Committee Briefing document.
X	20Feb2003		FDA Correspondence providing Pre-ACM Meeting Minutes.
X	04Mar2003		FDA Request for Clinical Information
X	06Mar2003		Gastrointestinal Drugs Advisory Committee Meeting
X	12Mar2003		FDA Version #1 of USPC (email)
X	14Mar2003		Teleconference (1) MRL/FDA to discuss: 1) Guidance from FDA on areas of particular concern for Phase IV; 2) Discussion of FDA proposed changes in the presentation and interpretation of pre-clinical carcinogenicity data in the EMEND USPC.
X	17Mar2003		FDA CMC/Labeling Information Request (facsimile)
X	17Mar2003		MRL Labeling Counterproposal to March 12, 2003 FDA Labeling. Included supplemental document addressing carcinogenicity section (email to FDA with electronic archival follow-up)
X	17Mar2003		FDA Version #1 of PPI (facsimile and email)

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
X	18Mar2003		MRL Facsimile to FDA containing Version #1 of Phase IV Commitments (facsimile for discussion purposes only, no archival copy)
X	18Mar2003		FDA Version #2 of USPC (email response to March 17, 2003 MRL labeling)
X	18Mar2003		MRL Response to FDA Request for Information [Proposed Post-Marketing Risk Management Program] (facsimile to FDA with electronic archival follow-up)
X	19Mar2003		Teleconference (2) MRL/FDA to discuss USPC (FDA Version #2 dated March 18, 2003)
X	19Mar2003		Teleconference MRL/FDA CMC Representatives to discuss March 17, 2003 CMC/Labeling Request for Information
X	19Mar2003		Teleconference (1) MRL/FDA to discuss Phase IV Commitments
X	19Mar2003		MRL Labeling Counterproposal (2) to March 18, 2003 FDA Labeling. Included two additional reference documents in support of labeling language for Carcinogenicity section. (email to FDA with electronic archival follow-up)
X	20Mar2003		Teleconference (3) MRL/FDA to discuss USPC (Review of MRL March 19, 2003 Counterproposal)
X	20Mar2003		MRL Facsimile to FDA containing Version #2 of Phase IV Commitments (facsimile for discussion purposes only, no archival copy)
X	20Mar2003		Teleconference (2) MRL/FDA to discuss Phase IV Commitments
X	20Mar2003		MRL Labeling Counterproposal (3, USPC) per discussions during March 20, 2003 Teleconference. (email to FDA with electronic archival follow-up)
X	20Mar2003		MRL Labeling Counterproposal (3, PPI) per discussions during March 20, 2003 Teleconference. (email to FDA with electronic archival follow-up)
X	20Mar2003		MRL Response to FDA CMC/Labeling Request for Information (email to FDA

IND 50,283 Serial No.	NDA 21-549	DATE	EVENT
			with electronic archival follow-up)
X	21Mar2003		Teleconference (4) MRL/FDA to discuss USPC (Review of MRL March 20, 2003 Counterproposal)
X	21Mar2003		MRL Response to FDA Request for Information - Phase IV Commitments (email to FDA with electronic archival follow-up)
X	21Mar2003		MRL Labeling Counterproposal (4, USPC & PPI) per discussions during March 20, 2003 Teleconference. (email to FDA with electronic archival follow-up)
283		21Mar2003	MRL Response to FDA Request for Information dated October 18, 2002.
X	24Mar2003		MRL Labeling Counterproposal (5, USPC) per discussions during March 20, 2003 Teleconference. (email to FDA with electronic archival follow-up)
X	26Mar2003		FDA Approval Letter, EMEND.